CLAIMS

What is claimed is:

1. A method for treating a patient in need of epinephrine, the method comprising:

administering an effective amount of substantially dry particles to the respiratory system of the patient, the particles comprising:

(a) epinephrine, or a salt thereof; and

(b) at least one pharmaceutically acceptable excipient.

2. The method of Claim 1, wherein the epinephrine, or salt thereof, is present in the particles in an amount ranging from about 1 to about 95 weight percent.

3. The method of Claim 2, wherein the epinephrine, or salt thereof, is present in the particles in an amount ranging from about 1 to about 45 weight percent.

4. The method of Claim 3, wherein the epinephrine, or salt thereof, is present in the particles in an amount ranging from about 1 to about 30 weight percent.

5. The method of Claim 1, wherein the particles are aerodynamically light.

6. The method of Claim 1, wherein the particles are spray dried.

7. The method of Claim 1, wherein the particles are substantially amorphous.

8. The method of Claim 1, wherein the epinephrine, or salt thereof, contained in the particles is substantially amorphous.

9. The method of Claim 1, wherein the epinephrine, or salt thereof, contained in the particles is substantially crystalline.

10. The method of Claim 1, wherein the pharmaceutically acceptable excipient contained in the particles is substantially amorphous.

11. The method of Claim 1, wherein the pharmaceutically acceptable excipient contained in the particles is substantially crystalline.

12. The method of Claim 1, wherein the particles are administered via inhalation.

13. The method of Claim 12, wherein the particles comprise at least about 50 micrograms of epinephrine and are administered in a single inhalation.

14. The method of Claim 13, wherein the particles comprise about 250 micrograms to about 5 milligrams of epinephrine and are administered in a single inhalation.

15. The method of Claim 1, wherein the particles are administered to the respiratory system via a breath activated inhaler.

16. The method of Claim 15, wherein the particles are administered to the respiratory system in a single breath activated step.

17. The method of Claim 1, wherein a first portion of the particles is deposited in the airways of the respiratory system and a second portion of the particles is deposited to the alveoli region of the lungs.

18. The method of Claim 1, wherein administering an effective amount of particles includes delivering a portion of the particles to the alveoli region of the lungs.

19. The method of Claim 1, wherein administering an effective amount of particles includes delivering a portion of the particles to the upper airways.

20. The method of Claim 1, wherein the epinephrine is released from the particles and acts systemically.

21. The method of Claim 1, wherein the epinephrine is released from the particles and acts locally.

22. The method of Claim 1, wherein the patient in need of epinephrine is suffering from anaphylaxis.

23. The method of Claim 1, wherein the patient in need of epinephrine exhibits at least one of the conditions selected from the group consisting of bronchoconstriction, bronchospasm, airway constriction, and edema.

24. The method of Claim 1, wherein the coefficient of variation for the maximum epinephrine concentration, C_{MAX}, in the patient's blood plasma of a dose of epinephrine is lower than for a non-intravenous injection of the same dose of epinephrine.

25. The method of Claim 24, wherein the non-intravenous injection is selected from the group consisting of a subcutaneous injection, an intramuscular injection, and an auto-injection.

26. The method of Claim 1, wherein the coefficient of variation for the time for maximum epinephrine concentration, T_{MAX}, in the patient's blood plasma of a dose of epinephrine is lower than for a non-intravenous injection of the same dose of epinephrine.

27. The method of Claim 26, wherein the non-intravenous injection is selected from the group consisting of a subcutaneous injection, an intramuscular injection, and an auto-injection.

28. The method of Claim 1, wherein the average time for maximum epinephrine concentration, T_{MAX}, in the patient's blood plasma of a dose of epinephrine is lower than for a non-intravenous injection of the same dose of epinephrine.

29. The method of Claim 26, wherein the non-intravenous injection is selected from the group consisting of a subcutaneous injection, an intramuscular injection, and an auto-injection.

30. The method of Claim 1, wherein the median time to maximum epinephrine concentration, T_{MAX}, in the patient's blood plasma is less than about 5 minutes.

31. The method of Claim 1, wherein the resulting epinephrine C_{MAX} in the patient's blood plasma is about 2 to about 3 times greater than epinephrine C_{MAX} in the patient's blood plasma provided by administration of a liquid-based aerosol.

32. The method of Claim 1, wherein the epinephrine is released from the particles in a sustained manner.

33. A method for treating a patient in need of epinephrine, the method comprising:

administering an effective amount of particles to the respiratory system of the patient, the particles comprising:

(a) epinephrine, or a salt thereof; and

(b) at least one pharmaceutically acceptable excipient;

wherein the effective amount of particles possess a fine particle fraction of less than 5.6 microns of at least about 45 percent.

34. A method for treating a patient in need of epinephrine, the method comprising:

administering an effective amount of particles to the respiratory system of the patient, the particles comprising:

(a) epinephrine, or a salt thereof; and

(b) at least one pharmaceutically acceptable excipient;

wherein the effective amount of particles possess a fine particle fraction of less than 3.4 microns of at least about 15 percent.

35. A method for treating a patient in need of epinephrine, the method comprising:

administering an effective amount of substantially dry particles to the respiratory system of the patient, the particles comprising epinephrine, or a salt thereof, and wherein a first portion of the particles is deposited in the airways of the respiratory system and a second portion of the particles is deposited to the alveoli region of the lungs.

36. The method of Claim 35, wherein the epinephrine, or salt thereof, is present in the particles in an amount ranging from about 1 to about 45 weight percent.

37. The method of Claim 36, wherein the epinephrine, or salt thereof, is present in the particles in an amount ranging from about 1 to about 30 weight percent.

38. The method of Claim 35, wherein the particles are aerodynamically light.

39. The method of Claim 35, wherein the particles are spray dried.

40. The method of Claim 35, wherein the particles comprise at least about 50 micrograms of epinephrine and are administered in a single inhalation.

41. The method of Claim 40, wherein the particles comprise about 250 micrograms to about 5 milligrams of epinephrine and are administered in a single inhalation.

42. The method of Claim 35, wherein the particles are administered to the respiratory system via a breath activated inhaler.

43. The method of Claim 35, wherein the particles are administered to the respiratory system in a single breath activated step.

44. The method of Claim 35, wherein the first portion of the particles is deposited at one or more sites of obstruction or constriction of the respiratory system.

45. The method of Claim 44, wherein the quantity of particles deposited at the one or more sites of obstruction or constriction of the respiratory system increases with the severity of obstruction or constriction.

46. The method of Claim 35, wherein epinephrine is locally released from the first portion of the particles that is deposited in the airways of the respiratory system.

47. The method of Claim 35, wherein epinephrine is released into the blood stream from the second portion of the particles that is deposited to the alveoli region of the lungs.

48. The method of Claim 35, wherein the patient in need of epinephrine is suffering from anaphylaxis.

49. The method of Claim 35, wherein the patient in need of epinephrine exhibits at least one of the conditions selected from the group consisting of bronchoconstriction, bronchospasm, airway constriction, and edema.

50. The method of Claim 35, wherein the coefficient of variation for the maximum epinephrine concentration, C_{MAX}, in the patient's blood plasma of a dose of epinephrine is lower than for a non-intravenous injection of the same dose of epinephrine.

51. The method of Claim 50, wherein the non-intravenous injection is selected from the group consisting of a subcutaneous injection, an intramuscular injection, and an auto-injection.

52. The method of Claim 35, wherein the coefficient of variation for the time for maximum epinephrine concentration, T_{MAX}, in the patient's blood plasma of a dose of epinephrine is lower than for a non-intravenous injection of the same dose of epinephrine.

53. The method of Claim 52, wherein the non-intravenous injection is selected from the group consisting of a subcutaneous injection, an intramuscular injection, and an auto-injection.

54. The method of Claim 35, wherein the average time for maximum epinephrine concentration, C_{MAX}, in the patient's blood plasma of a dose of epinephrine is lower than for a non-intravenous injection of the same dose of epinephrine.

55. The method of Claim 54, wherein the non-intravenous injection is selected from the group consisting of a subcutaneous injection, an intramuscular injection, and an auto-injection.

56. The method of Claim 35, wherein the median time to maximum epinephrine concentration, T_{MAX}, in the patient's blood plasma is less than about 5 minutes.

57. The method of Claim 35, wherein the resulting epinephrine C_{MAX} in the patient's blood plasma is about 2 to about 3 times greater than epinephrine C_{MAX} in the patient's blood plasma provided by administration of a liquid-based aerosol.

58. The method of Claim 35, wherein the epinephrine is released from the particles in a sustained manner.

59. A method for treating a patient in need of rescue therapy for anaphylaxis, the method comprising:

administering particles to the respiratory system of the patient, the particles comprising:

(a) a therapeutically effective amount of epinephrine, or a salt thereof; and

(b) at least one pharmaceutically acceptable excipient;

wherein the particles are delivered to the respiratory system and the epinephrine reaches its site of action within a time sufficiently short to provide said rescue therapy.

60. The method of Claim 59, wherein the epinephrine, or salt thereof, is present in the particles in an amount ranging from about 1 to about 45 weight percent.

61. The method of Claim 59, wherein the particles are aerodynamically light.

62. The method of Claim 59, wherein the particles are spray dried.

63. The method of Claim 59, wherein the particles comprise at least about 50 micrograms of epinephrine and are administered in a single inhalation.

64. The method of Claim 59, wherein the particles comprise about 250 micrograms to about 5 milligrams of epinephrine and are administered in a single inhalation.

65. The method of Claim 59, wherein the particles are administered to the respiratory system via a breath activated inhaler.

66. The method of Claim 59, wherein the particles are administered to the respiratory system in a single breath activated step.

67. The method of Claim 59, wherein a first portion of the particles is deposited in the airways of the respiratory system and a second portion of the particles is deposited to the alveoli region of the lungs.

68. The method of Claim 59, wherein the median time to maximum epinephrine concentration, T_{MAX}, in the patient's blood plasma is less than about 5 minutes.

69. A method for treating a patient suffering from anaphylaxis, the method comprising:

(a) administering an effective amount of substantially dry particles to the respiratory system of the patient, the particles comprising epinephrine, or a salt thereof;

(b) monitoring the patient; and

(c) administering additional epinephrine to the patient.

70. The method of Claim 69, wherein the particles comprise at least about 50 micrograms of epinephrine and are administered in a single inhalation.

71. The method of Claim 70, wherein the particles comprise about 250 micrograms to about 5 milligrams of epinephrine and are administered in a single inhalation.

72. The method of Claim 69, wherein the particles are administered to the respiratory system via a breath activated inhaler.

73. The method of Claim 72, wherein the particles are administered to the respiratory system in a single breath activated step.

74. The method of Claim 69, wherein a first portion of the dry particles is deposited in the airways of the respiratory system and a second portion of the dry particles is deposited to the alveoli region of the lungs.

75. The method of Claim 69, wherein the additional epinephrine is administered via inhalation.

76. The method of Claim 69, wherein the additional epinephrine is administered by a method selected from the group consisting of intramuscular injection, subcutaneous injection, auto-injection, and intravenous injection.

77. The method of Claim 69, wherein the particles or the additional epinephrine is self-administered.

78. The method of Claim 69, wherein the particles or the additional epinephrine are administered outside the direct supervision of a doctor or nurse.

79. The method of Claim 69, wherein the additional epinephrine is administered to the patient if symptoms of anaphylaxis continue substantially unabated for at least about 5 to about 30 minutes.

80. Particles for delivery of epinephrine to the respiratory system, the particles comprising:

(a) epinephrine, or a salt thereof;

(b) a carboxylic acid, or a salt thereof;

(c) a salt comprising at least one multivalent cation or anion; and

(d) a phospholipid.

81. A method for treating a patient in need of epinephrine, the method comprising:

administering an effective amount of particles to the respiratory system of a patient, the particles comprising:

(a) epinephrine, or a salt thereof;

(b) a carboxylic acid, or a salt thereof;

(c) a salt comprising at least one multivalent cation or anion; and

(d) a phospholipid.

82. Particles for delivery of epinephrine to the respiratory system, the particles comprising:

(a) epinephrine, or a salt thereof;

(b) an amino acid; and

(c) a sugar.

83. A method for treating a patient in need of epinephrine, the method comprising:

administering an effective amount of particles to the respiratory system of a patient, the particles comprising:

(a) epinephrine, or a salt thereof;

(b) an amino acid; and

(c) a sugar.

84. Particles for delivery of epinephrine to the respiratory system, the particles comprising:

(a) epinephrine, or a salt thereof; and

(b) an amino acid.

85. A method for treating a patient in need of epinephrine, the method comprising:

administering an effective amount of particles to the respiratory system of a patient, the particles comprising:

(a) epinephrine, or a salt thereof; and

(b) an amino acid.

86. Particles for delivery of epinephrine to the respiratory system, the particles comprising:

(a) epinephrine, or a salt thereof;

(b) an amino acid; and

(c) a carboxylic acid, or a salt thereof.

87. A method for treating a patient in need of epinephrine, the method comprising:

administering an effective amount of particles to the respiratory system of a patient, the particles comprising:

(a) epinephrine, or a salt thereof;

(b) an amino acid; and

(c) a carboxylic acid, or a salt thereof.

88. Particles for delivery of epinephrine to the respiratory system, the particles comprising:

(a) about 11 to about 21 weight percent epinephrine bitartrate;

(b) about 62 to about 82 weight percent leucine; and

(c) about 7 to about 17 weight percent sodium tartrate.

89. A method for treating a patient in need of epinephrine, the method comprising:

administering an effective amount of particles to the respiratory system of a patient, the particles comprising:

(a) about 11 to about 21 weight percent epinephrine bitartrate;

(b) about 62 to about 82 weight percent leucine; and

(c) about 7 to about 17 weight percent sodium tartrate.

90. Particles for delivery of epinephrine to the respiratory system, the particles comprising:

(a) about 12 to about 23 weight percent epinephrine bitartrate; and

(b) about 77 to about 88 weight percent leucine.

91. A method for treating a patient in need of epinephrine, the method comprising:

administering an effective amount of particles to the respiratory system of a patient, the particles comprising:

(a) about 12 to about 23 weight percent epinephrine bitartrate; and

(b) about 77 to about 88 weight percent leucine.

92. Spray dried particles for delivery of epinephrine to the respiratory system, the particles comprising:

(a) epinephrine, or a salt thereof; and

(b) at least one pharmaceutically acceptable excipient;

wherein the particles possess a fine particle fraction of less than 5.6 microns of at least about 45 percent.

93. Spray dried particles for delivery of epinephrine to the respiratory system, the particles comprising:

(a) epinephrine, or a salt thereof; and

(b) at least one pharmaceutically acceptable excipient;

wherein the particles possess a fine particle fraction of less than 3.4 microns of at least about 15 percent.

94. Essentially dry particles for delivery of epinephrine to the respiratory system, the particles comprising:

(a) epinephrine, or a salt thereof; and

(b) at least one pharmaceutically acceptable excipient.

95. The particles of Claim 94, wherein the particles are aerodynamically light.

96. The particles of Claim 94 ,wherein the particles are spray dried.

97. The particles of Claim 94, wherein the particles are substantially amorphous.

98. The particles of Claim 94, wherein the epinephrine, or salt thereof, contained in the particles is substantially amorphous.

99. The particles of Claim 94, wherein the epinephrine, or salt thereof, contained in the particles is substantially crystalline.

100. The particles of Claim 94, wherein the pharmaceutically acceptable excipient contained in the particles is substantially amorphous.

101. The particles of Claim 94, wherein the pharmaceutically acceptable excipient contained in the particles is substantially crystalline.

102. The particles of Claim 94, wherein the particles further comprise an antioxidant.

103. A propellent-free pharmaceutical composition comprising essentially dry particles for delivery of epinephrine to the respiratory system, wherein the particles comprise:

(a) epinephrine, or a salt thereof; and

(b) at least one pharmaceutically acceptable excipient.

104. A substantially antioxidant-free pharmaceutical composition comprising dry particles for delivery of epinephrine to the respiratory system, wherein the particles comprise:

(a) epinephrine, or a salt thereof; and

(b) at least one pharmaceutically acceptable excipient.

105. A method for treating a patient in need of epinephrine, comprising:

(a) administering an effective amount of a first mass of substantially dry particles to the respiratory system of the patient, the particles comprising epinephrine, or a salt thereof; and

(b) subsequently, administering an effective amount of a second mass of substantially dry particles to the respiratory system of the patient, the particles comprising epinephrine, or a salt thereof.

106. The method of Claim 105 wherein the first and second masses of substantially dry particles further comprise a pharmaceutically acceptable excipient.

107. The method of Claim 106 wherein the pharmaceutically acceptable excipient is leucine.

108. The method of Claim 105 wherein the first and second masses of substantially dry particles further comprise a carboxylic acid, or a salt thereof.

109. The method of Claim 108 wherein the first and second masses of substantially dry particles further comprise tartrate, or a salt thereof.

110. The method of Claim 105 wherein the first and second masses of substantially dry particles comprise

(a) about 11 to about 21 weight percent epinephrine bitartrate;

(b) about 62 to about 82 weight percent leucine; and

(c) about 7 to about 17 weight percent sodium tartrate.

111. The method of Claim 105 further comprising the administration of at least one additional effective amount of substantially dry particles to the respiratory system of the patient.

112. The method of Claim 105 wherein the first and second masses of substantially dry particles are delivered via a breath activated inhaler.

113. The method of Claim 112 wherein the first and second masses of substantially dry particles are delivered in single breath activated steps.

114. The method of Claim 105 wherein the effective amount of the first mass of substantially dry particles and the effective amount of the second mass of substantially dry particles are delivered via separate inhalation devices.

115. The method of Claim 105 wherein the first and second masses of substantially dry particles are delivered via a multi-dose inhalation device.

116. The method of Claim 105 wherein the effective amount of the first mass of substantially dry particles and the effective amount of the second mass of substantially dry particles are delivered via a single inhalation device.

117. The method of Claim 105 wherein the effective amount of the second mass of substantially dry particles is administered at least about 5 minutes after the effective amount of the first mass of substantially dry particles.

118. The method of Claim 117 wherein the effective amount of the second mass of substantially dry particles is administered at least about 10 minutes after the effective amount of the first mass of substantially dry particles.

119. The method of Claim 105 wherein the effective amount of the second mass of substantially dry particles is administered before the symptoms of anaphylaxis have substantially abated.

120. The method of Claim 105 wherein the effective amount of the second mass of substantially dry particles is administered within about 24 hours of administration of the effective amount of the first mass of substantially dry particles.

121. The method of Claim 105 wherein the patient in need of epinephrine is experiencing anaphylaxis.

122. The method of Claim 121 wherein the second effective amount of substantially dry particles is administered during a single episode of anaphylaxis.

123. The method of Claim 105 wherein the effective amount of the second mass of substantially dry particles is administered while the patient experiences at least one of the conditions selected from the group consisting of bronchoconstriction, bronchospasm, airway constriction, and edema.

124. A method for treating a patient suffering from anaphylaxis, comprising:

(a) administering an effective amount of a first mass of substantially dry particles to the respiratory system of the patient, the particles comprising epinephrine, or a salt thereof; and

(b) subsequently, administering an effective amount of a second mass of substantially dry particles to the respiratory system of the patient, the particles comprising epinephrine, or a salt thereof;

wherein the first and second masses of substantially dry particles comprise

(a) about 11 to about 21 weight percent epinephrine bitartrate;

(b) about 62 to about 82 weight percent leucine; and

(c) about 7 to about 17 weight percent sodium tartrate.

125. The method of Claim 124 wherein the effective amount of the first mass of substantially dry particles comprises about 500 micrograms of epinephrine.

126. The method of Claim 124 wherein the effective amount of the second mass of substantially dry particles comprises about 500 micrograms of epinephrine.

127. The method of Claim 124 wherein the effective amount of the second mass of substantially dry particles is administered within about 30 minutes of the administration of the effective amount of the first mass of substantially dry particles.

128. The method of Claim 124 wherein the effective amount of the first mass of substantially dry particles comprises about 500 micrograms of epinephrine, the effective amount of the second mass of substantially dry particles comprises about 500 micrograms of epinephrine, and the effective amount of the second mass of substantially dry particles is administered about 10 to about 20 minutes after administration of the effective amount of the first mass of substantially dry particles.

129. The method of Claim 124 wherein the first and second masses of substantially dry particles comprise

(a) about 16 weight percent epinephrine bitartrate;

(b) about 72 weight percent leucine; and

(c) about 12 weight percent sodium tartrate.

130. A method for treating a patient in need of epinephrine, the method comprising:

administering an effective amount of substantially dry particles to the respiratory system of the patient, the particles comprising epinephrine, or a salt thereof.

131. The method of Claim 130 wherein the particles are aerodynamically light.

132. The method of Claim 130 wherein the particles are spray dried.

133. The method of Claim 130 wherein the particles are administered via inhalation.

134. The method of Claim 133 wherein the particles are administered to the respiratory system via a breath activated inhaler.

135. The method of Claim 133 wherein the particles are administered to the respiratory system in a single breath activated step.

136. The method of Claim 130 wherein the patient in need of epinephrine is suffering from anaphylaxis.

137. A method for treating a patient in need of epinephrine, the method comprising:

administering an effective amount of particles to the respiratory system of the patient, the particles comprising epinephrine, or a salt thereof; wherein the effective amount of particles possess a fine particle fraction of less than 5.6 microns of at least about 45 percent.

138. A method for treating a patient in need of epinephrine, the method comprising:

administering an effective amount of particles to the respiratory system of the patient, the particles comprising epinephrine, or a salt thereof; wherein the effective amount of particles possess a fine particle fraction of less than 3.4 microns of at least about 15 percent.

139. A method for treating a patient in need of rescue therapy for anaphylaxis, the method comprising:

administering particles to the respiratory system of the patient, the particles comprising a therapeutically effective amount of epinephrine, or a salt thereof;

wherein the particles are delivered to the respiratory system and the epinephrine reaches its site of action within a time sufficiently short to provide said rescue therapy.